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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

ROBINSON, HOPE A

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 01/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/529,925

Applicant(s)

Georges et al.

Examiner

HOPE ROBINSON

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Oct 21, 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6, 7, 15-27, 30-33, and 37-40 is/are pending in the application.
- 4a) Of the above, claim(s) 6, 7, 24-27, 30, and 31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-23, 32, 33, and 37-40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 17 6) ☐ Other: _____

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DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 21, 2002 has been entered. It is noted that applicant filed a new Declaration and Informational Disclosure Statement.

Claim Disposition

2. Claims 34-36 have been canceled. Claims 37-40 have been added. Claims 15, 18-20 and 22-23 have been amended. Claims 15-23, 32-33 and 37-40 are under examination.

3. The following grounds of rejection are or remain applicable :

Specification

4. The specification is objected to because of the following informalities:

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The specification is objected to because on page 1 of the specification does not disclose the priority information.

Correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 15-23, 32-33 and 37- 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 and all other claims reciting this language are indefinite/unclear with regard to candidate compound altering of resistance. The compound is recited in the claim preamble as “directly” affecting Annexin-based MDR, however, it is not apparent whether or not a method in which cell membrane integrity is compromised would or would not be considered direct; or, does direct mean one to one physicochemical interaction of the candidate drug with the biological

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agent effecting MDR? How does the claim distinguish directly from indirectly? It is not readily apparent where in the specification that “directly” is defined. See also claims 37 and 39.

Claim 16 is indefinite because the claim does not further limit claim 15, as each of the limitations recited in claim 15 appears in dependent claim 16. Claim 15 recites “an expression of annexin” and claim 16 recites “expression from a nucleic acid molecule”, however, claim 15 would have reasonably had annexin expression from a nucleic acid molecule and explicit recitation in claim 16 does not further limit the claim.

Claims 17 and 18 are indefinite with regard to the Markush listing. The claims recite “a nucleic acid molecule encoding an Annexin variant, **or part thereof, a dominant negative mutant of an Annexin, a mutant Annexin, an antibody to Annexin a peptide**, and a small molecule”. Note that the Markush listing is confusing and inconsistent (with regard to administration of a protein as opposed to administration of a polynucleotide), extraneous commas which separate phrases inappropriately, double inclusion (with regard to mutant annexin and dominant negative mutant annexin which is included in the broad term “mutant annexin”), and reference to an antibody to annexin a peptide.

Claims 17 and 20 remain indefinite because the claims recite “small molecule”, as this terminology is not specific as to the identity of the material proposed.

Claim 32 and all other claims with this language are indefinite because the claim recites “increase in the expression of an annexin protein, whereby said increased expression is capable of conferring MDR”, as applicant on pages 11-12 of the response states that over-expression of a

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gene in a cell displaying a specific phenotype is not reliable proof that the gene causes this phenotype. Thus, it appears applicant statement contradicts the invention as claimed.

Claims 19, 21-23, 33, 38 and 40 are indefinite as the claims depend from a rejected based claim.

6. Applicant's response was not sufficient to overcome this ground of rejection. For example, applicant contends that the term "small molecule" is well known in the art, however, the references provided as a means of support refer to a specific small molecule unlike the present claims. See for example, the reference submitted by Ecker et al., 1999, where it is stated that "RNA is a small molecule". The claims remain vague and indefinite because it is unclear the metes and bounds of the claim, as to what applicant intends "small molecule" to mean. The references provided named several types of small molecules that may not be the ones claimed which provides support that the claim is indefinite. Furthermore, the references do not define what is considered to be a small molecule neither does the instant specification. Note that new grounds of rejections have also been instituted under this statute.

Claim Rejections - 35 U.S.C. § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103 (a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103 (a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102 (f) or (g) prior art under 35 U.S.C. 103 (a).

8. Claims 15, 16, 17, 19-20 and 37-40 32 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Wang et al.

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(Biochemical and Biophysical Research Communications, vol. 236, pages 483-488, 1997) based on the disclosure which states that P-40 is Annexin I and that the invention relates to the identification of Annexins (I-XI, also referred to herein as P-40 and P-40 homologs (see page 4 of the specification).

Wang disclose a method comprising the binding of IMP96 to P-40 in MCF-7/Adr cells (see Figure 1) and demonstrates that P-40 (Annexin I) confers resistance to Taxol and Adriamycin (see Table 1). Wang further discloses that the over expression of P-40 in paclitaxel or cis-platinum selected cell lines, in the absence of a detectable level of P-gp or MRP supports the notion that P-40 alone may confer resistance to cytotoxic drugs (see page 486). Wang also disclose that P-40 could modulate an MDR phenotype indirectly, by stating that P-40 may be a component of the apoptosis signaling pathway. Moreover, Wang discloses that changes in the levels or functions of proteins involved in the signaling of apoptosis can confer an MDR phenotype on tumor cells (see page 487). Wang also disclose a method that identifies a protein that mediates drug resistance to anticancer drugs. Wang further discloses a method that was used to isolate a monoclonal antibody (IPM96) which recognized a protein (P-40) co-expressed with P-glycoprotein in several resistant cell lines. Additionally, Wang discloses that over expression of P-40 (protein which is Annexin) in multidrug resistant cells may be important in the expression of the drug resistance phenotype (see pages 483-485).

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The Wang reference anticipates the claimed invention as Wang identifies a compound (P-40) that affects Annexin-based MDR in a cell in the presence of a drug (Adriamycin and Taxol) and assessed the effect of said compound as claimed in the present application. Further, Wang discloses a method that utilizes an antibody to Annexin and a compound that modulates Annexin based MDR in a cell as the present application discloses that P-40 and Annexin are equivalent. Although Wang does not teach a direct correlation as recited in claim 15, it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention as a whole because Wang teaches that there is an indirect correlation and that P-40 is important in the expression of drug resistance phenotype, thus provides a suggestion for a direct correlation. Furthermore, it is not apparent whether or not a method in which cell membrane integrity is compromised would or would not be considered to be “direct”. Thus, the claimed invention was obvious to make and use at the time it was made and was *prima facie* obvious.

9. Applicant's arguments filed on October 21, 2002 in Paper No. 15 have been fully considered but were not persuasive. The basis of applicant's arguments with regard to the art rejection is that the claims have now been amended to recite a “direct decrease” (see for example claim 15). Applicant then contends that the Wang reference does not teach this direct correlation. Note that the rejection of record has been withdrawn in favor of a rejection under 35 U.S.C. 102/103. Applicant is directed to the reasoning provided under 35 U.S.C. 112, second

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paragraph with regard to the insertion of “direct” into the claims. As it is not apparent whether or not a method in which cell membrane integrity is compromised would or would not be considered to be direct the Wang reference remains relevant. Furthermore, Wang provides a suggestion of such a relationship, thus, the claimed invention was obvious to make and use. Note also that newly submitted claims 37-40 are also obvious over the Wang reference for the reasons stated above. The references submitted by applicant have been considered regarding issues around “over expression”, however, the standards of the 103(a) statute only requires a mere teaching or suggestion thus, the Wang reference remains relevant. Note that claim 32 appears to contradict applicant’s statements. Additionally, one of skill in the art would be motivated to arrive at the claimed invention via Wang’s teachings because Wang indicates that further investigation would lead to a direct correlation.

Applicant’s response pointed out that newly submitted claims 32 and 33 were not examined. Based on this inadvertent error, an examination of these two claims appears in this office action.

Conclusion

10. No claims are allowable.


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Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Hope A. Robinson whose telephone number is (703)308-6231. The Examiner can normally be reached on Monday and Wednesday- Friday from 9:00 A.M. to 5:30 P.M. (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor Christopher S.F. Low, can be reached at (703)308-2932.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703)308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-2742. Please affix the Examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope A. Robinson, MS 

Patent Examiner


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